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09/926,154	12/26/2001	Toshiaki Tagawa	P21462	2932

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EXAMINER

COUNTS, GARY W

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/926,154

Applicant(s)

TAGAWA ET AL.

Examiner

Gary W. Counts

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-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,2 and 4-26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 4-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### **Status of the claims**

The amendment filed December 29, 2003 is acknowledged and has been entered.

### **Remarks**

The request for withdrawal of finality of office action filed December 29, 2003 is acknowledged and has been found persuasive. Applicant's remarks that the rejection of claims 2, 7, 20 and 24 under 35 U.S.C 103(a) as being unpatentable over Allen in view of Tagawa was not included in the previous Office Action, and is raised upon unamended claims in the present Final Office Action is found persuasive and therefore the finality of the office action is withdrawn and entry of the amendment filed December 29, 2003 is acknowledged.

### ***Claim Objections***

1. Claim 1 is objected to because of the following informalities: the recitation bond in line 5 and line 7 should be --bound--. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1, 2, and 4-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, line 3 the recitation "generally" is a relative term which renders the claim indefinite. The term "generally" is not defined by the claim, the specification

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does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 1, line 3 the recitation "can generally be" is vague and indefinite. The recitation is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. Is the free target recognized by the ligand at equivalent level as the non-free target when not bound to the microparticle or not?

Claim 1, line 4 the recitation "substantially" is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 1, line 5 "said at least one ligand comprising plural numbers of the at least one ligand bound to a surface of the microparticle" is vague and indefinite because it is unclear if the ligand comprises plural numbers of ligands or if the microparticle comprises plural numbers of the ligand on its surface. Please clarify.

Claim 1, line 7 the recitation "a surface" is vague and indefinite. It is unclear if applicant is referring to the same surface recited in line 5 or if applicant is referring to some other surface.

### ***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 2, 5, 7-14, 16, 17, 19-22, and 24-26 are rejected under 35

U.S.C. 102(b) as being anticipated by Tagawa et al (US 5,264,221).

Tagawa et al disclose a liposome (microparticle) bonded to at least one antibody (ligand). Tagawa et al disclose that this antibody can be a human monoclonal antibody directed to MKN 45 (non-free target) (col 7 & 8). Tagawa et al disclose polyalkylene glycol (water-soluble macromolecule) bonded to the liposomes. Tagawa et al disclose polyethylene glycol (PEG)-modified liposomes (col 2, lines 1-40). Tagawa et al disclose the liposome can comprise adrimaycin (col 3).

With respect to “the at least one ligand comprising plural numbers” as recited in the instant claims. One skilled in the art would recognize that the liposome of Tagawa et al would comprise more than one of the antibodies on its surface. Therefore, Tagawa et al teaches plural numbers of the ligand. Further, since there would be more than one antibody on the surface of the liposome (same as recited in the instant claims). The liposome of Tagawa would possess increased affinity to the non-free target.

With respect to “the ligand having affinity for both a free target and a non-free target so that the free target can generally be recognized by the ligand at substantially equivalent level as the non-free target when not bound to the microparticle” as recited in the instant claims. Since Tagawa et al teaches that the ligand can be a human monoclonal antibody directed to MKN 45 (human gastric cancer cell) (same type of antibody that applicant discloses on page 4, line 20, a human cancer cell-reactive monoclonal antibody). The ligand of Tagawa et al would possess the property of having

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affinity for both a free target and a non-free target so that the free target can generally be recognized by the ligand at substantially equivalent level as the non-free target when no bound to the microparticle.

Further, Since Tagawa teaches the same type of antibody (human cancer cell-reactive human monoclonal antibody) directed to the same antigen (MKN 45), Tagawa et al disclose the ligand-bonded complex as claimed and therefore, it would inherently comprise the increasing affinity of the at least one ligand bound to a surface of the microparticle allowing specific bind of the complex to a non-free target in the presence of both a non-free target and a free target as recited in the instant claims.

With respect to the dissociation constant between the target and one ligand as recited in the instant claims. Tagawa et al disclose the ligand-bonded complex as claimed and therefore, it would inherently comprise the dissociation constant between the target and one ligand as recited in the instant claims.

6. Claims 1, 2, 4, 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Li et al (US 5,512,294).

Li et al disclose liposomes (microparticles) derivitized with antibodies (ligand). Li et al disclose that these antibodies can be VCAM-1 antibodies directed to VCAM-1 (col 5 and col 10, lines 4-45). Li et al disclose that the liposomes can comprise plural numbers of the antibody bound to its surface (see Figure 16). Li et al disclose that these antibodies can be indirectly or directly bound to the liposome (col 10, lines 4-45).

With respect to "the ligand having affinity for both a free target and a non-free target so that the free target can generally be recognized by the ligand at substantially

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equivalent level as the non-free target when not bound to the microparticle” as recited in the instant claims. Since Li et al teaches that the ligand can be anti-VCAM-1 (same type of antibody that applicant discloses on page 17 of the specification). It appears that the ligand of Li et al would possess the property of having affinity for both a free target and a non-free target so that the free target can generally be recognized by the ligand at substantially equivalent level as the non-free target when no bound to the microparticle.

Li et al disclose the ligand-bonded complex as claimed and therefore, it would inherently comprise the increasing affinity of the at least one ligand bound to a surface of the microparticle allowing specific bind of the complex to a non-free target in the presence of both a non-free target and a free target as recited in the instant claims.

With respect to the dissociation constant between the target and one ligand as recited in the instant claims. Li et al disclose the ligand-bonded complex as claimed and therefore, it would inherently comprise the dissociation constant between the target and one ligand as recited in the instant claims.

### ***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining

obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 6, 15 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tagawa et al in view of Allen et al (US 5,527,528).

See above for teachings of Tagawa et al.

Tagawa et al differ from the instant invention in failing to specifically teach that the at least one ligand molecule is indirectly bonded to the microparticle by polyethylene glycol.

Allen et al disclose liposomes containing an anti-tumor compound in liposome entrapped form. Allen et al disclose monoclonal antibodies coupled to the liposome by

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polyethylene glycol chains (col 2 & col 4, lines 17-67). Allen et al disclose that the coupling of antibodies to the peg molecule allows the antibody in the polymer layer to be positioned at a selected depth in the layer, as shown to increase or decrease the extent to which the antibody is buried in the polymer layer (col 4, lines 51-60). Allen et al also disclose that these peg-coupled antibodies provide liposomes with an extended blood circulation time to a site to obtain greater therapeutic activity of a liposome-entrapped compound (col 3).

It would have been obvious to one of ordinary skill in the art to couple antibodies to polyethylene glycol molecules as taught by Allen et al into the liposome of Tagawa et al because Allen et al shows that the coupling of antibodies to the peg molecule allows the antibody in the polymer layer to be positioned at a selected depth in the layer, as shown to increase or decrease the extent to which the antibody is buried in the polymer layer. Allen et al also shows that these peg-coupled antibodies provide liposomes with an extended blood circulation time to a site to obtain greater therapeutic activity of a liposome-entrapped compound (col 3).

11. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tagawa et al in view of Lindhofer et al (US 6,294,167).

See above for teachings of Lindhofer et al.

Tagawa et al differ from the instant invention in failing to teach the ligand-bounded complex in a pharmaceutical composition.

Lindhofer et al disclose immunoliposomes which have monoclonal antibodies bound on their surfaces. Lindhofer et al disclose that these immunoliposomes are contained in

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pharmaceutical compositions (col 6). Lindhofer et al disclose that these compositions provide for particular tumor cells, to be distinguished from other cells on account of the recognition of specific marker antigens and are therefore suitable for immunological cell therapy and the pharmaceutical compositions lend themselves to in vivo and in vitro therapy of different tumor types (col 1).

It would have been obvious to one of ordinary skill in the art to incorporate pharmaceutical compositions as taught by Lindhofer et al with the liposomes of Tagawa et al because Lindhofer et al shows that these compositions provide for particular tumor cells, to be distinguished from other cells on account of the recognition of specific marker antigens and are therefore suitable for immunological cell therapy and the pharmaceutical compositions lend themselves to in vivo and in vitro therapy of different tumor types.

### ***Response to Arguments***

12. Applicant's arguments with respect to claims 1, 2 and 4-26 concerning Allen et al and Buechler et al have been considered but are moot in view of the new ground(s) of rejection.

### ***Conclusion***


No claims are allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Gary Counts  
Examiner  
Art Unit 1641  
February 5, 2004

  
**LONG V. LE**  
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02/20/04